REMARKS

I. Status of the claims

Claims 38-43 are pending and currently stand rejected. Applicants acknowledge and thank the Examiner for the indication that "any rejections or objections of record not explicitly addressed [in the Office Action mailed May 26, 2009], are hereby withdrawn, in light of applicant's arguments and/or the *Amendments to the Claims,* filed April 6, 2009." Office Action at 3.

II. New Specification Objection

A. Specification

The Office Action at pages 3 and 4 recite suggested guidelines for the arrangement of the specification. The Office Action concludes that "Appropriate correction is **required**." Office Action at 4 (emphasis added). However, Applicants are not aware of any requirement to follow those guidelines. The specification complies with statutory sections such as 35 U.S.C. § 112, and hence Applicants respectfully decline to follow the guidelines proposed by the Office, particularly since adverse consequences in any subsequent litigation can possibly result from adopting the Office's suggestion.

B. Title

The Office has objected to the title of the present application as not being descriptive. Accordingly, Applicants have amended the title to recite "4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline, its pharmaceutically acceptable salts, and pharmaceutical

compositions comprising the same." The title as amended describes the presently claimed inventions. In response to the Office's suggestion, Applicants are not aware of any requirement to recite alleged utility in a title. Accordingly, Applicants' respectfully decline to include any recitation of utility in the title. Withdrawal of the present objection is respectfully requested.

III. New Claim Objections

The Office, at page 4, objects to claims 38 and 41, indicating that "and its pharmaceutically acceptable salts" should be replaced with "or its pharmaceutically acceptable salts." Applicants respectfully disagree with the Office, and traverse this objection.

The M.P.E.P. states that an applicant may use "alternative expressions.. or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought." M.P.E.P. § 2173.01. In this case, the phrase "a compound chosen from 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline and its pharmaceutically acceptable salts" is proper language and accurately describes boundaries of the claimed invention, *i.e.,* the compound may be:

(1) 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline,

(2) a pharmaceutically acceptable salt of 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline,

(3) more than one pharmaceutically acceptable salt of 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline,

(4) 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline and a pharmaceutically acceptable salt of 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline, or

(5) 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline and more than one a pharmaceutically acceptable salt of 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]-oxy}quinazoline.

The present claim language is clear, and the Office has not demonstrated otherwise. Nor has the Office shown any legal basis for requiring Applicants to change the claim language. Accordingly, Applicants respectfully request that the Office withdraw the claim objections.

IV. Rejection Under 35 U.S.C. § 103(a)

Claims 38-43 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,924,285 ("Himmelsbach"). Office Action at 5-8. Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, one of ordinary skill in the art must have had a reason to attempt to make the claimed composition or compound. See M.P.E.P. § 2143.

The Office asserts that Himmelsbach discloses the 3-chloro-4-fluoro analog of the presently claimed 3-chloro-2-fluoro compound (hereinafter referred to as "Example (38)"). The Office also asserts that the M.P.E.P. states that position isomers are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. Office Action at 6. The Office also asserts that "it is well established that position isomers are structurally prima facie obvious, even in the absence of a teaching to modify." *Id.* Applicants respectfully disagree; the generalizations made by the Office fail to constitute a *prima facie* case of obviousness. In particular, those generalizations fail to provide a reason to attempt to make the claimed composition or compound and hence are improper under M.P.E.P. § 2143.

Indeed, subsequently to *KSR Int'l Co. v. TeleFlex Inc.,* 127 S.Ct. 1727 (2007), the Federal Circuit, in a number of cases,[1] has elaborated upon the requirements for establishing a prima facie case of obviousness in cases involving alleged structural similarity.

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[1] *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.,* 492 F.3d 1350 (Fed. Cir. 2007),
Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd., 533 F.3d 1353 (Fed. Cir. 2008),
The Procter & Gamble Company v. Teva Pharmaceuticals USA, Inc. , __ F.3d __, No. 2008-1404, -1405, -1406 (Fed. Cir. May 13, 2009), and
In re Kubin, __ *F.3d* __, No. 2008-1184, (Fed. Cir. Apr. 3, 2009).

For example, in *Takeda Chemical Industries, Ltd., v. AlphaPharm Pty, Ltd.*, 492 F.3d 1350, 1356, (Fed. Cir. 2007), made of record on the attached SB08, the Court asserted (emphasis added):

> [a] known compound may suggest its homolog, analog, or isomer because such compounds 'often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.' *Id.* We clarified, however, that **in order to find a prima facie case of unpatentability in such instances, a showing that the 'prior art would have suggested making the *specific* molecular modifications necessary to achieve the claimed invention' was also required.**

In other words,

> Obviousness based on structural similarity thus can be proved by identification of **some motivation that would have led one of ordinary skill in the art to *select and then modify* a known compound (i.e. a lead compound) *in a particular way*** to achieve the claimed compound.

Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd., 533 F.3d 1353, 1357, 87 U.S.P.Q.2D (BNA) 1452 (Fed. Cir. 2008) (citing *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007)) (emphasis added).

A Reasoned Identification of a Lead Compound is Required But Has Not Been Made

An obviousness argument based on structural similarity between claimed and prior art compounds "clearly depends on a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound] as a lead compound." *The Procter & Gamble Company v. Teva Pharmaceuticals USA, Inc.* , __ F.3d __, No. 2008-1404, -1405, -1406, slip op. at 6 (Fed. Cir. May 13, 2009) (*citing Takeda*, 492 F.3d at 1359 and *Eisai,* 533 F.3d at 1359 (emphasis added) (stating that "post-*KSR*, a prima

facie case of obviousness for a chemical compound still, in general, **begins with the reasoned identification of a lead compound**" in the prior art; "First, ***KSR* assumes a starting reference point or points in the art**, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions.")).

There Would Have Been No Reason to Select Himmelsbach's Example (38) as a Lead Compound

Himmelsbach's broadest genus encompasses hundreds of thousands, if not millions, of quinazoline compounds. As will be discussed below, other than improper hindsight, nothing in Himmelsbach would have suggested the selection of Example (38) as the lead compound for further modification. And no reason has been provided by the Office for doing so either.

Himmelsbach discloses sixteen (16) synthetic examples that can be used to make over 150 different compounds. *See* Examples 1-16. Himmelsbach also discloses over 180 additional compounds that "may also be prepared analogously to the foregoing Examples and other methods known from the literature." *See* columns 56-128. Although Example (38) is one of those over 330 compounds, Himmelsbach's specification, when viewed as a whole, actually teaches away from selecting Example (38) as a lead compound.

For example, Example (38) is not one of those described in Himmelsbach as one of the "most particularly preferred compounds of general formula I" described in columns 8-11, line 5, or the "particularly preferred compounds" from col. 11, line 7 to column 12, line 12, nor is Example (38) one of the 22 "examples of particularly preferred compounds of general formula I" recited by name in columns 12-13 and claimed in

claim 6. Furthermore, Himmelsbach provides biological data for 26 compounds, but none of those is Example (38). See column 19, line 50 to column 20, line 15.

Accordingly, one of ordinary skill in the art would not have selected Example (38) as a lead compound. Rather, Himmelsbach teaches away from Example (38) and to at least 22 compounds having a different structure from Example (38). Applicants thus respectfully request withdrawal of this rejection.

Applicants note the Office's warning that

> although not explicitly discussed herein, applicant is advised to note that the Himmelscach reference contains additional species that may obviate 4-(3-chloro-2-fluoroanilino)-7-methoxy-6-{[l-(N-methylcarbamoylmethyl)piperidin-4-yl]oxy}quinazoline. Consequently, any amendments to the claims to overcome rejections rendered under 35 U.S.C. § 103(a) should address this reference as a whole and should not be limited to the species discussed or disclosed explicitly herein.

Office Action at 8.

However, that warning does not apply because no amendments are made herein at all, let alone to overcome the obviousness rejection. Furthermore, the Office carries the initial burden of presenting a prima facie case of obviousness. M.P.E.P. § 2142. It is the Office's burden to make the "reasoned identification" of a lead compound, per *Eisai, supra*. The Office has failed to do that, and hence Applicants have no duty to address the non-obviousness of species other than that cited by the Examiner, Example (38), at this time. Accordingly, Applicants respectfully request withdrawal of the present rejection.

V. Provisional Nonstatutory Obviousness-Type Double Patenting Rejection

Claims 38-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-35 of copending Application No. 12/147,250. Applicants respectfully traverse this rejection.

The Office asserts that, although the conflicting claims are not identical, they are not patentably distinct from each other because claims 24-35 in the copending application recites definitions for G^1, G^2, X^1, X^2, R^1 and Q^1which provide **overlapping subject matter** with respect to the instant claims. Office Action at 9 (emphasis added).

To be sure, claim 38 falls within the literal scope of claims of Application No. 12/147,250. But that fact alone does not establish obviousness-type double patenting of claim 38, particularly in the context of the present application. With respect to such a situation, the M.P.E.P. cautions:

> **Domination and double patenting should not be confused.** They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. **Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection**.

M.P.E.P. § 804(II) (*citing In re Kaplan,* 789 F.2d 1574, 1577-78 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, (CCPA 1964)) (emphasis added).

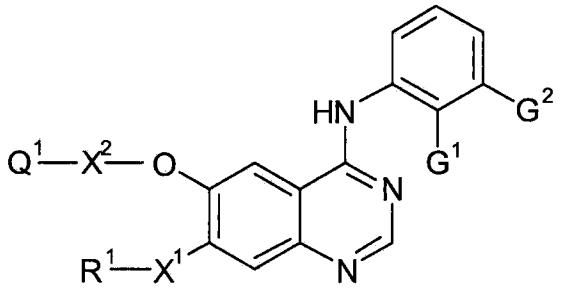
Hence, it is not enough that claims of the copending application encompass the subject matter of claims 38-43. Rather, to support an obviousness-type double patenting rejection, claims 24-35 of Application No. 12/147,250 **must have rendered obvious the present claims 38-43**.

"A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is 'analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103' except that the patent principally underlying the double patenting rejection is not considered prior art." M.P.E.P. § 804(II)(B)(1) (citing *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967)). "Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination." *Id.* (citing *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985)).

As shown below, present claim 38 is patentably distinct over the claims of that copending application due to the breadth of the copending claims, and, as in *Baird*, the total lack of suggestion in the lost count to select the presently claimed compound/salts recited in present claims 38-43.

Copending Claims 24-35 With Present Claim 38 Overlap Highlighted

24. A quinazoline of Formula I:

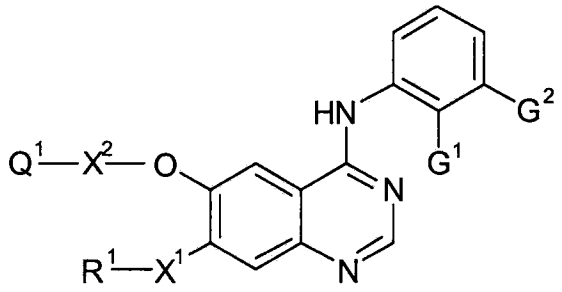


wherein:
G^1 and G^2 each independently is halogeno;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is heterocyclyl, wherein Q^1 optionally bears 1 or 2 substituents, which may be the same or different, selected from carbamoyl, (1-6C)alkyl, (1-6C)alkylsulphonyl, N-(1-6C)alkylcarbamoyl,

N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, and N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, and wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from hydroxy, and/or optionally a substituent selected from (1-6C)alkoxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, or R^a and R^b together with the nitrogen atom to which they are attached form a 5 or 6 membered ring, which optionally bears 1 or 2 substituents on an available ring carbon atom selected from (1-4C)alkyl;
or a pharmaceutically acceptable salt thereof.

25. A quinazoline according to claim 24, wherein Q^1 is heterocyclyl, optionally bearing 1 or 2 substituents, which may be the same or different, selected from carbamoyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, and N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, and wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from NR^aR^b, wherein R^a is hydrogen and R^b is hydrogen;
or a pharmaceutically acceptable salt thereof.

26. At least one compound chosen from (a) quinazolines of Formula I:

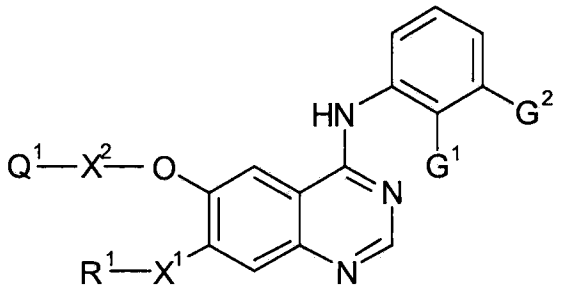


wherein:
G^1 and G^2 each independently is halogeno;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is heterocyclyl, wherein Q^1 optionally bears 1 or 2 substituents, which may be the same or different, selected from carbamoyl, (1-6C)alkyl, (1-6C)alkylsulphonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, and N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, and

wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from hydroxy, and/or optionally a substituent selected from (1-6C)alkoxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, or R^a and R^b together with the nitrogen atom to which they are attached form a 5 or 6 membered ring, which optionally bears 1 or 2 substituents on an available ring carbon atom selected from (1-4C)alkyl;
and (b) pharmaceutically acceptable salts thereof.

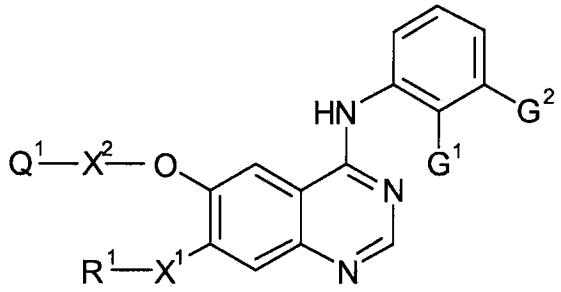
27. At least one compound according to claim 26, wherein in said quinazolines (a),
Q^1 is heterocyclyl, optionally bearing 1 or 2 substituents, which may be the same or different, selected from carbamoyl, (1-6C)alkyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]-carbamoyl, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, and N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl,
and wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from NR^aR^b, wherein R^a is hydrogen and R^b is hydrogen;
and (b) pharmaceutically acceptable salts thereof.

28. A quinazoline of Formula I:



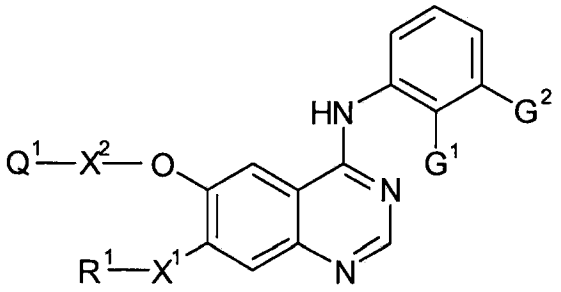
wherein:
G^1 and G^2 each independently is chosen from fluoro and chloro;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is linked to X^2 -O by a ring carbon atom and is a heterocyclyl chosen from pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl, piperidin-4-yl, piperidin-3yl, piperidin-2yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, piperazin-3-yl, and 1,2,3,6-tetrahydropyridin-4-yl, wherein Q^1 bears 1 or 2 substituents selected from N-(1-6C)alkylcarbamoyl and N-(1-6C)alkylcarbamoyl(1-6C)alkyl,
or a pharmaceutically acceptable salt thereof.

29. At least one compound chosen from (a) quinazolines of Formula I:



wherein:
G^1 and G^2 each independently is chosen from fluoro and chloro;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is linked to X^2-O by a ring carbon atom and is a heterocyclyl chosen from pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl, piperidin-4-yl, piperidin-3yl, piperidin-2yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, piperazin-3-yl, and 1,2,3,6-tetrahydropyridin-4-yl, wherein Q^1 bears 1 or 2 substituents selected from: N-(1-6C)alkylcarbamoyl, (1-6C)alkyl, and N-(1-6C)alkylcarbamoyl(1-6C)alkyl, and (b) pharmaceutically acceptable salts thereof.

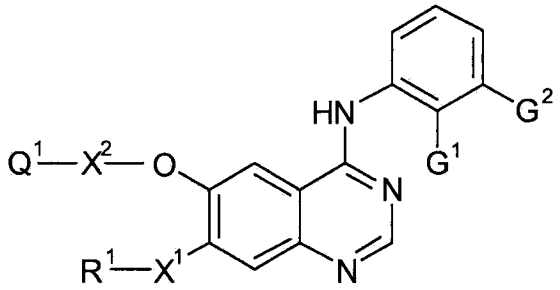
30. A quinazoline of Formula I:



wherein:
G^1 and G^2 each independently is halogeno;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is a non-aromatic saturated 5 or 6 membered monocyclic heterocyclyl ring with at least one nitrogen atom, which ring is linked to the group X^2-O- by a carbon atom in the ring,

wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from hydroxy, and/or optionally a substituent selected from (1-6C)alkoxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, or R^a and R^b together with the nitrogen atom to which they are attached form a 5 or 6 membered ring, which optionally bears 1 or 2 substituents on an available ring carbon atom selected from (1-4C)alkyl;
or a pharmaceutically acceptable salt thereof.

31. A quinazoline of Formula I:

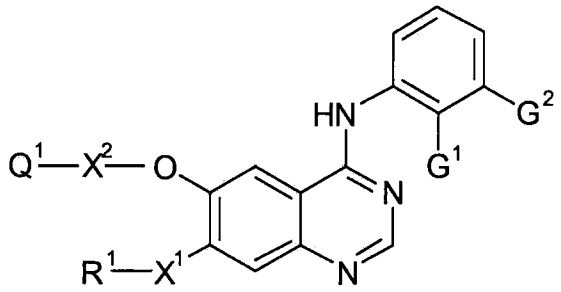


wherein:
G^1 and G^2 each independently is halogeno;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is a non-aromatic saturated 4, 5 or 6 membered monocyclic heterocyclyl ring with 1 or 2 ring nitrogen heteroatom(s), which ring is linked to the group X^2-O- by a ring carbon atom,

wherein any (1-6C)alkyl and (2-6C)alkanoyl group within Q^1 optionally bears one or more substituents, which may be the same or different, selected from hydroxy, and/or optionally a substituent selected from (1-6C)alkoxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, or R^a and R^b together with the nitrogen atom to which they are attached form a 5 or 6 membered ring, which optionally bears 1 or 2 substituents on an available ring carbon atom selected from (1-4C)alkyl;
or a pharmaceutically acceptable salt thereof.

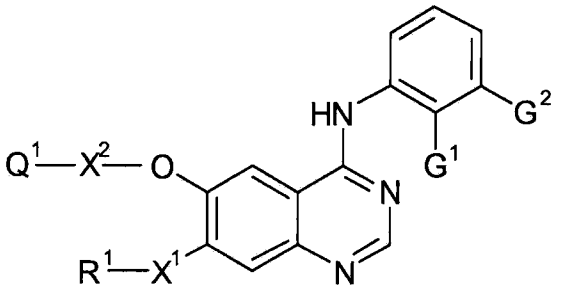
32. The quinazoline of Formula I according to claim 31, wherein in said quinazolines (a),
Q^1 is selected from pyrrolidin-3-yl, pyrrolidin-2-yl, piperidin-4-yl, piperidin-3-yl, piperidin-2-yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, and piperazin-3-yl
and (b) pharmaceutically acceptable salts thereof.

33. A quinazoline of Formula I:



wherein:
G^1 is fluoro and G^2 is chloro;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is linked to X^2 -O by a ring carbon atom and is a heterocyclyl chosen from pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl, piperidin-4-yl, piperidin-3-yl, piperidin-2yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, piperazin-3-yl, and 1,2,3,6-tetrahydropyridin-4-yl, and
wherein Q^1 bears 1 or 2 substituents selected from N-(1-6C)alkylcarbamoyl and N-(1-6C)alkylcarbamoyl(1-6C)alkyl,
or a pharmaceutically acceptable salt thereof.

34. A quinazoline of Formula I:

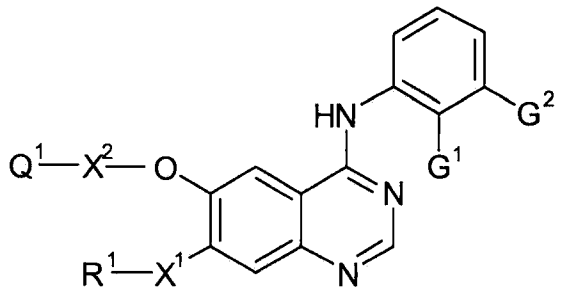


wherein:
G^1 and G^2 each independently is chosen from fluoro and chloro;
X^1-R^1 is methoxy;
X^2 is a direct bond;
Q^1 is linked to X^2 -O by a ring carbon atom and is a heterocyclyl chosen from pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl, piperidin-

4-yl, piperidin-3yl, piperidin-2yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, piperazin-3-yl, and 1,2,3,6-tetrahydropyridin-4-yl, and

wherein Q^1 bears 1 or 2 substituents selected from N-(1-6C)alkylcarbamoyl and N-(1-6C)alkylcarbamoyl(1-6C)alkyl, or a pharmaceutically acceptable salt thereof.

35. A quinazoline of Formula I:



wherein:
G^1 and G^2 each independently is chosen from fluoro and chloro;
X^1 is O;
R^1 is (1-4C)alkyl;
X^2 is a direct bond;
Q^1 is linked to X^2 -O by a ring carbon atom and is a heterocyclyl chosen from pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl, piperidin-4-yl, piperidin-3yl, piperidin-2yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-2-yl, piperazin-3-yl, and 1,2,3,6-tetrahydropyridin-4-yl, and

wherein Q^1 bears 1 or 2 substituents selected from N-(1-6C)alkylcarbamoyl and N-(1-6C)alkylcarbamoyl(1-6C)alkyl, or a pharmaceutically acceptable salt thereof.

The Office, focusing on claim 33, asserts that

> if R^1 is -CH3 and Q^1 is piperidin-4-yl, optionally substituted with $-CH_2C(O)NHCH_3$ [N-(1-6C)alkylcarbamoyl(1-6C)alkyl], in claim 33 of the copending application, then the recited species of the copending application is identical to the species recited in the instant application, *4-(3-chloro-2-fluoroanilino-7-methoxy-6-{[1-(N-methylcarbamoyl-methyl)piperidin-4-yl]oxy}-quinazoline.*

Office Action at 9-10.

However, in claim 33 of the copending Application No. 12/147,250, Q^1 may be any of 11 different groups. In contrast, Q^1 in present claim 38 is the single heterocyclyl, piperidin-4-yl.

In claim 33 of the copending Application No. 12/147,250, Q^1 may be mono- or di-substituted with substituent(s) chosen from 2 classes of groups comprising 42 different groups (the class of N-(1-6C)alkylcarbamoyl groups comprises 6 groups and the class of N-(1-6C)alkylcarbamoyl(1-6C)alkyl groups comprises 36 different groups). However, in present claim 38, Q^1 bears the single substituent N-methyl-carbamoylmethyl.

There are hundreds of thousands of possibilities in claim 33 of the continuation, estimated as folllows:

- R^1 may (1-4C)alkyl, thus there are seven possible compounds including branched alkyls.
- Q^1 may be chosen from 11 different groups. Thus, 77 (11 times 7) compounds are possible.
- Furthermore, Q^1 may be substituted by 1 or 2 substituents selected from N-(1-6C)alkylcarbamoyl and N-(1-6C)alkylcarbamoyl(1-6C)alkyl. Thus, Q^1 may be substituted by 1 or 2 substituents selected from 42 substituents.
- Taking 77 compounds, as discussed above, and multiplying by the number of possible single substituents (42) means 3,234 compounds would be encompassed by claim 33.
- Taking 77 compounds, as discussed above, and multiplying by the number of possible double substituents (42 squared = 1764) means 135,828 compounds

plus the 3,234 compounds if Q^1 were singly-substituted means that claim 33 would encompass 139,062 compounds.

And there are numerous pharmaceutically acceptable salts of those compounds disclosed, resulting in an even larger number reaching into the hundreds of thousands. *See,e.g.,* p. 19, lines 5-12 of PCT parent published as WO 2003/082831 and para. [0062] US Published Application No. 2008/0269487 (the US publication of the AZ continuation). Nothing in any of the copending claims 24-35 in any way suggests or directs toward the species and its salts recited in claim 38.

Accordingly, due to the breadth of claim 33 and the lack of any guideposts or blaze marks in claim 33, or any other claim, of the copending application leading to the narrower, present claim 38, claim 38 is not rendered obvious by claim 33 or by any of claims 24-32, 34, and 35.

Applicants' also believe that the present claims 39-43 would not have been obvious in view of claims 24-35 of Application No. 12/147,250 for essentially the same reasons that claim 38 is not obvious in view of claim 33 of the copending application, or any other claim of the copending application.

For the foregoing reasons, Applicants respectfully request that the obviousness-type double patenting be withdrawn.

VI. Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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